Fabrication of 3D Cardiac Microtissue Arrays using Human iPSC-Derived Cardiomyocytes, Cardiac Fibroblasts, and Endothelial Cells.

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Public Summary:
Generation of human cardiomyocytes (CMs), cardiac fibroblasts (CFs), and endothelial cells (ECs) from induced pluripotent stem cells (iPSCs) has provided a unique opportunity to study the complex interplay among different cardiovascular cell types that drives tissue development and disease. In the area of cardiac tissue models, several sophisticated three-dimensional (3D) approaches use induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) to mimic physiological relevance and native tissue environment with a combination of extracellular matrices and crosslinkers. However, these systems are complex to fabricate without microfabrication expertise and require several weeks to self-assemble. Most importantly, many of these systems lack vascular cells and cardiac fibroblasts that make up over 60% of the nonmyocytes in the human heart. Here we describe the derivation of all three cardiac cell types from iPSCs to fabricate cardiac microtissues. This facile replica molding technique allows cardiac microtissue culture in standard multi-well cell culture plates for several weeks. The platform allows user-defined control over microtissue sizes based on initial seeding density and requires less than 3 days for self-assembly to achieve observable cardiac microtissue contractions. Furthermore, the cardiac microtissues can be easily digested while maintaining high cell viability for single-cell interrogation with the use of flow cytometry and single-cell RNA sequencing (scRNA-seq). We envision that this in vitro model of cardiac microtissues will help accelerate validation studies in drug discovery and disease modeling.

Scientific Abstract:
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